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NARRATIVE LITERATURE REVIEW

Retinal arterial macroaneurysms

Macroaneurisma arterial retiniano

Macroaneurisma arterial retiniano

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ABSTRACT

Retinal arterial macroaneurysms (RAMs) are commonly observed in the posterior pole, usually in the first arterial bifurcations, up to third-order vessels or arteriovenous crossings. Most RAMs are asymptomatic, with loss of vision occurring owing to hemorrhages or exudation with macular involvement. In general, RAM occurs in individuals aged 60–80 years, especially in women. Systemic arterial hypertension, age over 60 years, and the female sex are the main associated risk factors. The diagnosis is made based on ophthalmoscopy findings. Fluorescein angiography, indocyanine green angiography, and optical coherence tomography contribute to confirm the diagnosis. In this review article, we have described the epidemiology, pathogenesis, clinical presentation, findings of additional exams, differential diagnosis, systemic associations, pathology, treatment, and prognosis of RAM.

Keywords: Aneurysm; Retina; Hypertension; Eye Manifestations.

RESUMO

Os macroaneurismas arteriais retinianos (MAR) são comumente observados no pólo posterior, em geral nas primeiras bifurcações arteriais, até ramos de terceira ordem ou cruzamentos arteriovenosos. A maioria dos MAR são assintomáticos e a perda visual decorre de hemorragias ou exsudação com envolvimento macular. Geralmente, os MAR ocorrem em indivíduos entre 60 e 80 anos, preferencialmente do sexo feminino. A hipertensão arterial sistêmica, idade acima de 60 anos e o sexo feminino são os principais fatores de risco associados. O diagnóstico é feito pelos achados oftalmoscópicos. A angiografia fluoresceínica, a angiografia com indocianina verde e a tomografia de coerência óptica contribuem para confirmação diagnóstica. Neste artigo de revisão descreveremos a epidemiologia e patogênese, o quadro clínico, os achados de exames complementares, diagnóstico diferencial, associações sistêmicas, patologia, assim como tratamento e prognóstico.

Palavras-chave: Aneurisma; Retina; Hipertensión; Manifestaciones Oculares.

RESUMEN

Los macroaneurismas arteriales retinianos (MAR) son comúnmente observados en el polo posterior, en general en las primeras bifurcaciones arteriales, hasta ramas de tercera orden o cruces arteriovenosos. La mayoría de los MAR son asintomáticos y la pérdida visual adviene de hemorragias o exudación con comprometimiento macular. Generalmente, los MAR ocurren en individuos entre 60 y 80 años, preferencialmente del sexo femenino. La hipertensión arterial sistémica, la edad por encima de los 60 años y el sexo femenino son los principales factores de riesgo asociados. El diagnóstico se hace mediante hallazgos oftalmoscópicos. La angiografía fluoresceínica, la angiografía con indocianina verde y la tomografía de coherencia óptica aportan para confirmación diagnóstica. En este artículo de revisión, describiremos la epidemiología y la patogénesis, el cuadro clínico, los hallazgos de exámenes complementarios, diagnóstico diferencial, asociaciones sistémicas, patología, así como tratamiento y pronóstico.

Palabras Clave: Aneurisma; Retina; Hipertensión; Manifestaciones Oculares.

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INTRODUCTION

Retinal arterial macroaneurysms (RAMs) are characterized by round or fusiform dilations of retinal arteries, which are usually unilateral and single and are located within the first arterial bifurcations, up to third-order branches or arteriovenous crossings at the posterior pole. Most RAMs are asymptomatic, and loss of vision occurs owing to hemorrhages or exudation with macular involvement[1]. Robertson described this condition in 1973[2] and named it retinal macroaneurysm owing to its size, which was larger than that of microaneurysms observed in diabetic retinopathy and retinal vein occlusion.

EPIDEMIOLOGY AND PATHOGENESIS

In general, RAM occurs in individuals aged 60–80 years, predominantly in females. Systemic arterial hypertension is commonly present (65%–75% patients) along with other risk factors for stroke and coronary heart diseases, such as arteriosclerosis and dyslipidemia[3,4].

In a study conducted with 43 patients and 52 identified RAM paired with a similar control group, which aimed to identify ocular and systemic risk factors for RAM[5], the findings confirmed that RAM is predominantly present in females, and there was a higher prevalence of arterial hypertension and retinal vein occlusion in group comprising patients than that comprising controls. The author observed a 12 times higher risk of RAM being located in an area affected by vein occlusion[5]. In another study, which analyzed 147 patients, an association between macroaneurysm and the area affected by retinal vein occlusion was observed; the following four categories of retinal macroaneurysms were determined: arterial, venous, capillary, and collateral-associated. A distinct characteristic of this RAM group was retinal neovascularization in 32% of the eyes[6].

In a literature review, in which 60 patients with RAM were analyzed, RAM was predominantly present in females, reaching 80% of the sample. The mean age was 71 years, and systemic arterial hypertension was the most frequent associated finding (78% of cases)[7].

Changes related to arterial hypertension and aging may explain the emergence of RAM, for example, substitution of the mu/scular middle layer of the arterial wall by collagen, hyaline degeneration of the vessel wall, endothelial lesion by atheromas with thickening of the vascular lumen, increased vascular stiffness, and increased intravascular and transmural pressure. The loss of local self-regulation and turbulence occurs later with dilation of focal artery and formation of the macroaneurysm[7]. Weakening of the arterial wall leads to focal dilation and formation of the aneurysm[8,9].

There is histological evidence that local thromboembolic phenomena trigger the process that leads to the rupture of the macroaneurysm, with dissection of the inner vessel wall progressing to complete thickness[8].

CLINICAL FINDINGS

The temporal region is the predominant location of RAM, although arteries in the nasal region may also be affected[3].

In an assessment of the location of RAM in 34 patients, the following percentages were obtained: 50% in the superior temporal region, 44.7% in the inferior temporal region, and 5.2% in the nasal vessels[10].

Similar findings were obtained in another study, in which 21 symptomatic RAMs were evaluated, with the following distribution: 52.4% in the superior temporal region, 38% in the inferior temporal region, and 9.6% in the nasal region[11].

Macroaneurysms may develop less commonly in the cilioretinal artery[12] (Figure 1).

Other findings of this study were as follows: retinal hemorrhage in 81% of the samples, retinal exudates in 70%, vitreous hemorrhage in 30%, macular involvement in 30%, and distal arteriolar narrowing in 26%. Spontaneous arteriolar occlusion occurred in 8% samples and in 16% samples after laser photocoagulation[5].

The visual acuity distribution among 60 patients with RAM was as follows: 23% with 20/40 or better, 18% from 20/50 to 20/80, 43% worse than 20/200, and 28% at counting fingers. Half of the patients had a hemorrhagic presentation, and 10% of these had vitreous hemorrhage and 39% presented sub- or preretinal hemorrhage. Macular edema was found in 33% of the cases[6]. The presence of hemorrhage at multiple levels (retinal, subretinal, and preretinal or vitreous) strongly suggests the presence of RAM, although it may also occur in cases of age-related macular degeneration (AMD) of the exudative type[7] (Figure 2).

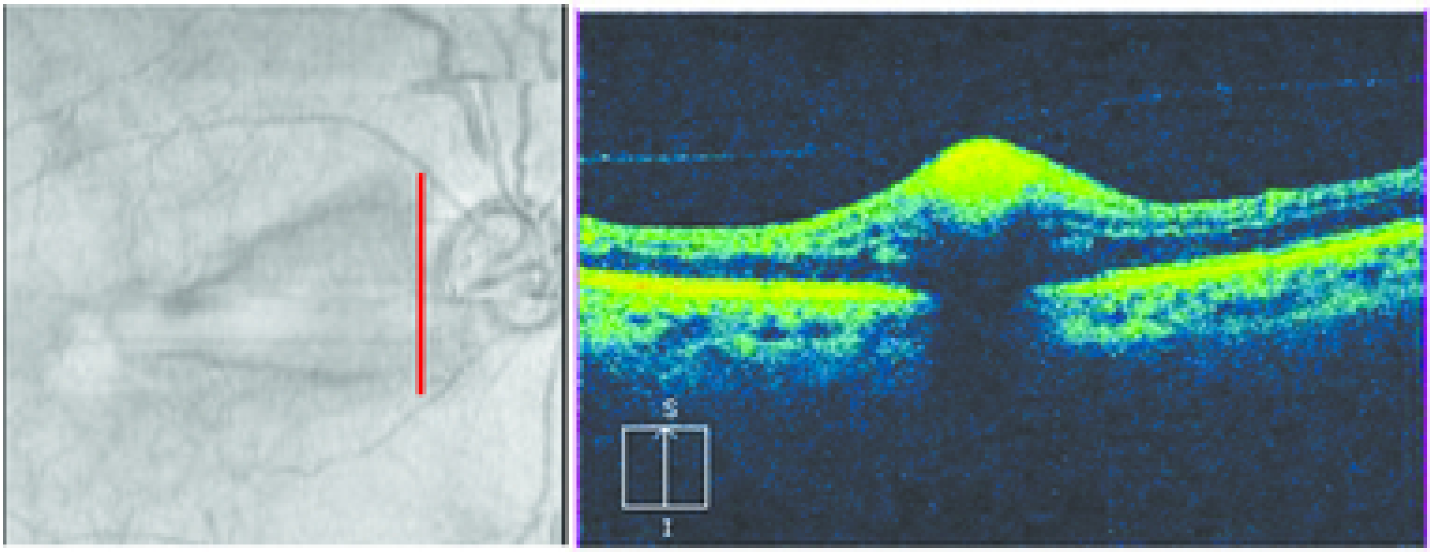


Figure 1. Optical coherence tomography image of a RAM in the cilioretinal artery.

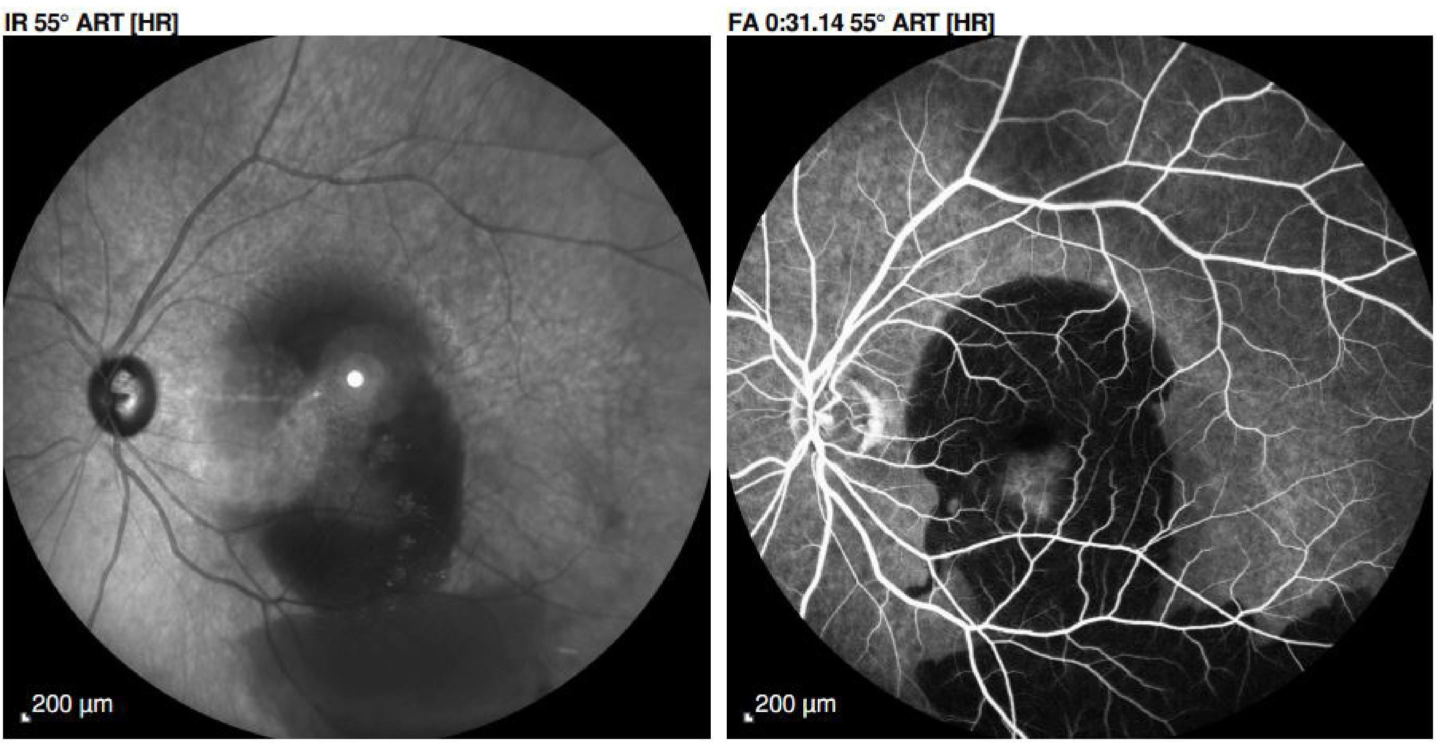


Figure 2. Red-free fundus photography and fluorescein angiography with extensive hypofluorescence owing to hemorrhagic blocking related to an occult subretinal neovascular membrane (courtesy of Dr. Diego Fleury).

DIAGNOSIS AND ADDITIONAL EXAMS

In most cases, arterial macroaneurysms can be diagnosed by clinical examination of the fundus. Fluorescein angiography and optical coherence tomography (OCT) can also assist in the investigation.

Fluorescein angiography

The macroaneurysm is filled with contrast early during the angiogram, presenting itself as a fusiform hyperfluorescence in the shape of a light bulb (Figure 3). In the late phases, its appearance varies from contrast impregnation of the vessel wall to extravasation.

Changes in the retinal capillaries can be observed by fluorescein angiography. Some RAMs present a visible pulsation. The significance of this finding concerning the risk for hemorrhagic complications is uncertain[13].

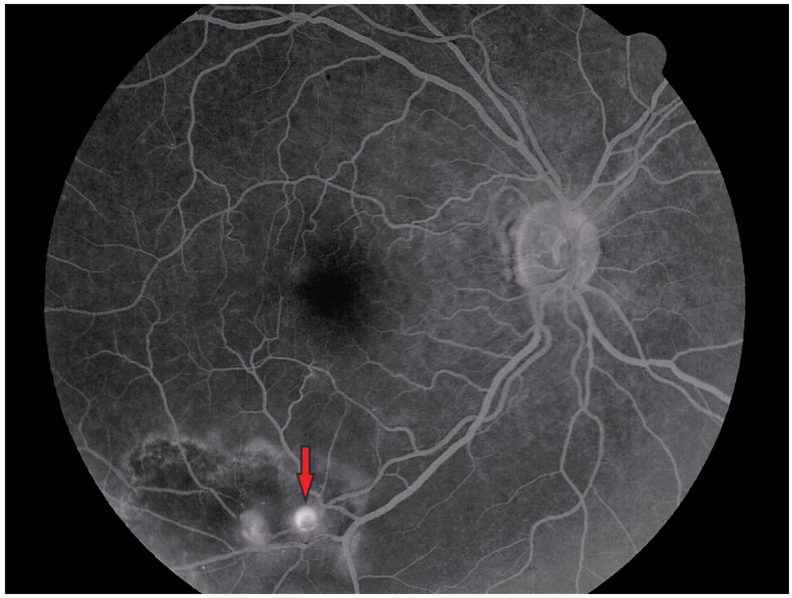


Figure 3. Fluorescein angiography showing an inferior temporal retinal arterial macroaneurysm (red arrow), with its typical light bulb shape.

Vitreous hemorrhage from RAM has been documented during retinal fluorescein angiography. Some eyes exhibit yellow plaques (atheroma) near RAM and other retinal arteries (Figure 4).

When associated with retinal venous occlusions, retinal ischemia and neovascularization areas may be observed, characterized by progressive leakage[5] (Figure 5).

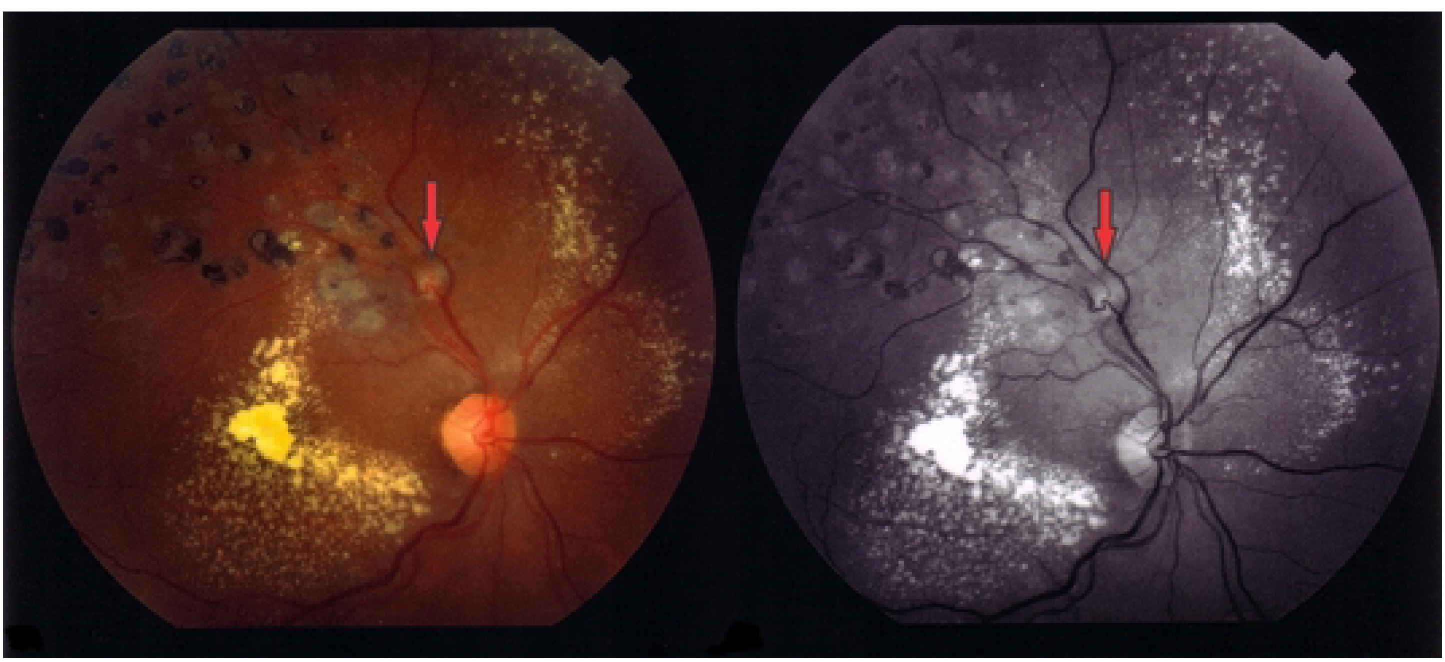


Figure 4. Colored and red-free fundus photography. Diffuse arterial involvement owing to hypertensive and atheromatous disease. Superior temporal macroaneurysm (red arrows).

Indocyanine green angiography

Fluorescein angiography examination is often hindered by the blocking caused by the adjacent hemorrhage that may cover or surround the macroaneurysm (Figure 6). In half of these cases, the diagnosis can be made by fluorescein angiography alone; however, with the use of indocyanine green, which is able to cross the hemorrhagic block, 75%–100% RAMs are diagnosed, showing a pulsatile arterial dilation[15-17].

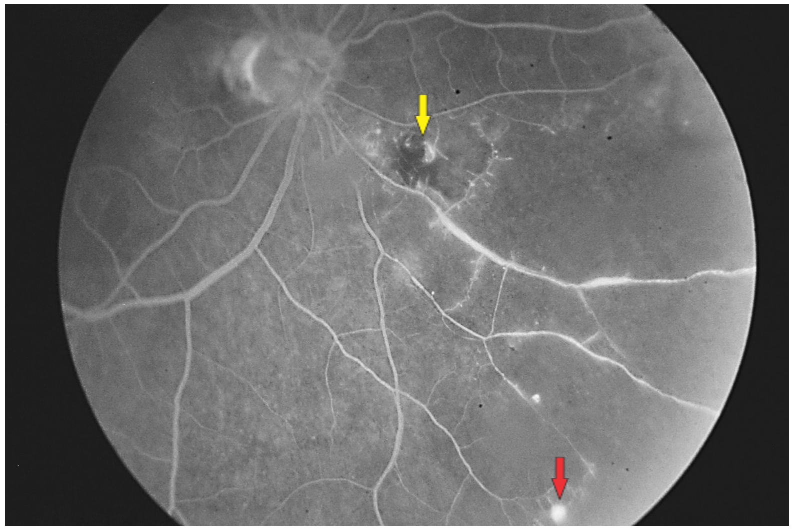


Figure 5. Fluorescein angiography. Macroaneurysm (yellow arrow) in the area of retinal venous occlusion, with ischemia revealed by hypofluorescence owing to capillary loss and hyperfluorescent retinal neovascularization (red arrow).

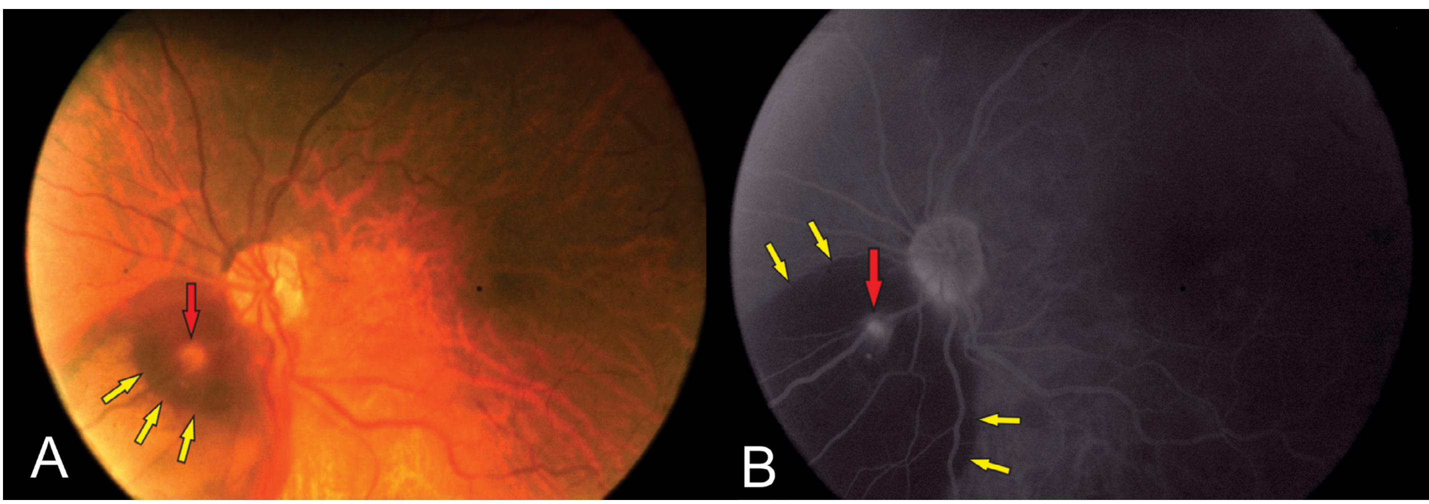


Figure 6. A) Color fundus photography showing a nasal RAM (red arrow) below the optic disc, surrounded by subretinal hemorrhage (yellow arrows). B) Fluorescein angiography of the same eye showing RAM (red arrow), with a round and hyperfluorescent appearance and subretinal hemorrhage in its margin (yellow arrows) causing hypofluorescence owing to the blocking.

Optical Coherence Tomography (OCT)

OCT of the lesion shows thickening of the area with increased vascular lumen. The macroaneurysm can be objectively identified and measured (Figure 7).

When the macroaneurysm is surrounded by hemorrhage, it is possible to notice the contrast between the raised area and macroaneurysm, similar to a valley between two summits (Figure 8).

This examination is of great importance to identify complications such as macular edema and serous retinal detachment, which are related to a worse visual prognosis owing to the possibility of irreversible lesion of the retinal outer layers (Figure 9).

Subretinal hemorrhages are shown with hyperreflectivity on the examination[18,19] (Figure 10).

Angio-OCT allows observing the flow inside RAM, which distinguishes thrombosed RAM from patent RAM[20].

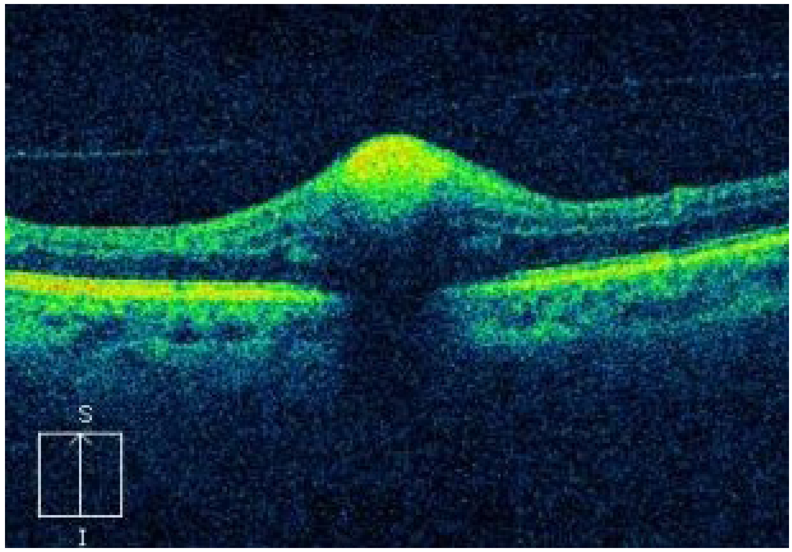


Figure 7. Optical coherence tomography (OCT). Optical section in the macroaneurysm area, evidenced by a round lesion at the center of the section, with an image of posterior attenuation.

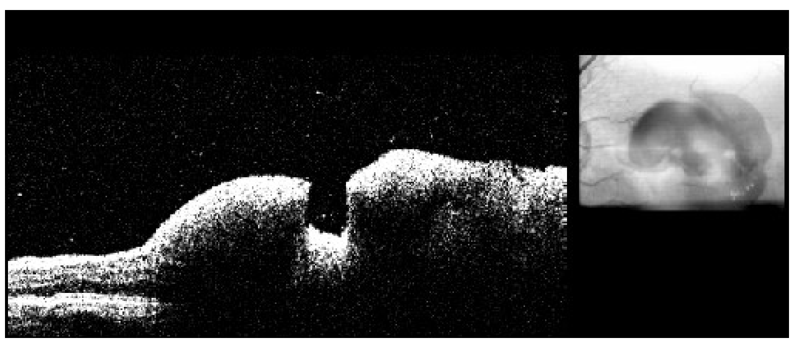


Figure 8. Optical coherence tomography (OCT). Optical section in the macroaneurysm area (central deep area), surrounded by sub- and preretinal hemorrhage ("valley" sign).

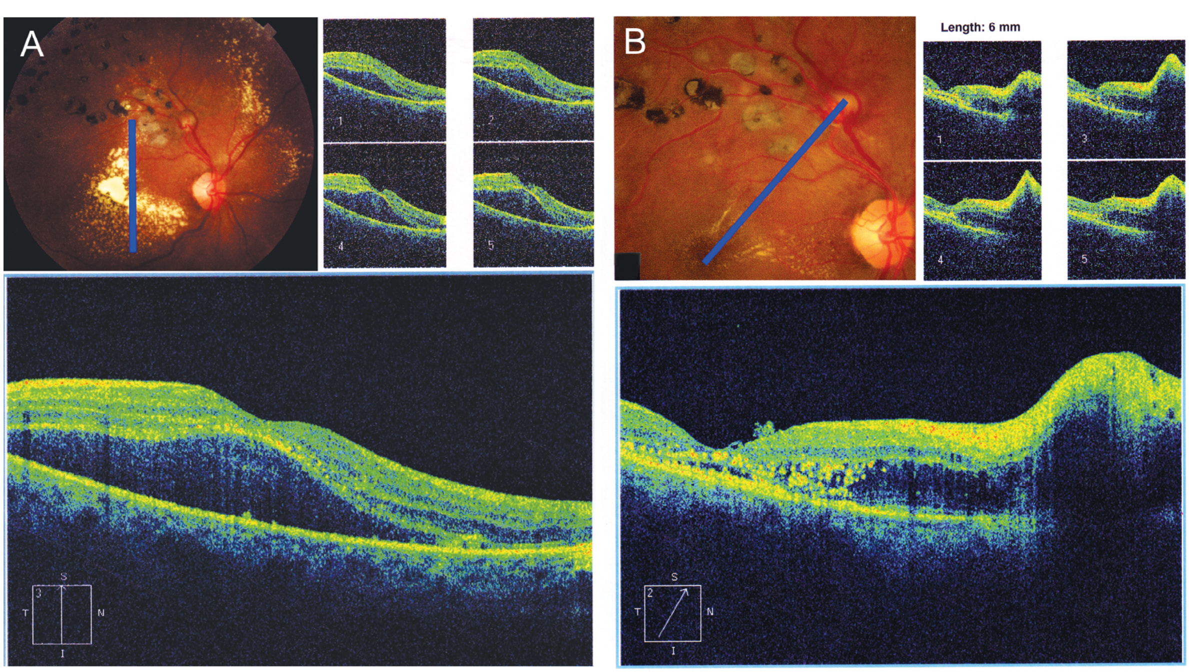


Figure 9. Optical coherence tomography (OCT). Optical section (blue lines) in the macular region and the RAM area. A 63-year-old female patient with RAM that progressed after an old vein occlusion photocoagulated. It progressed to an exuberant macular edema. Images before (6A) and 6 months after (6B) treatment with three intravitreal injections of ranibizumab at monthly intervals. The presence of intra- and subretinal fluid can also be observed.

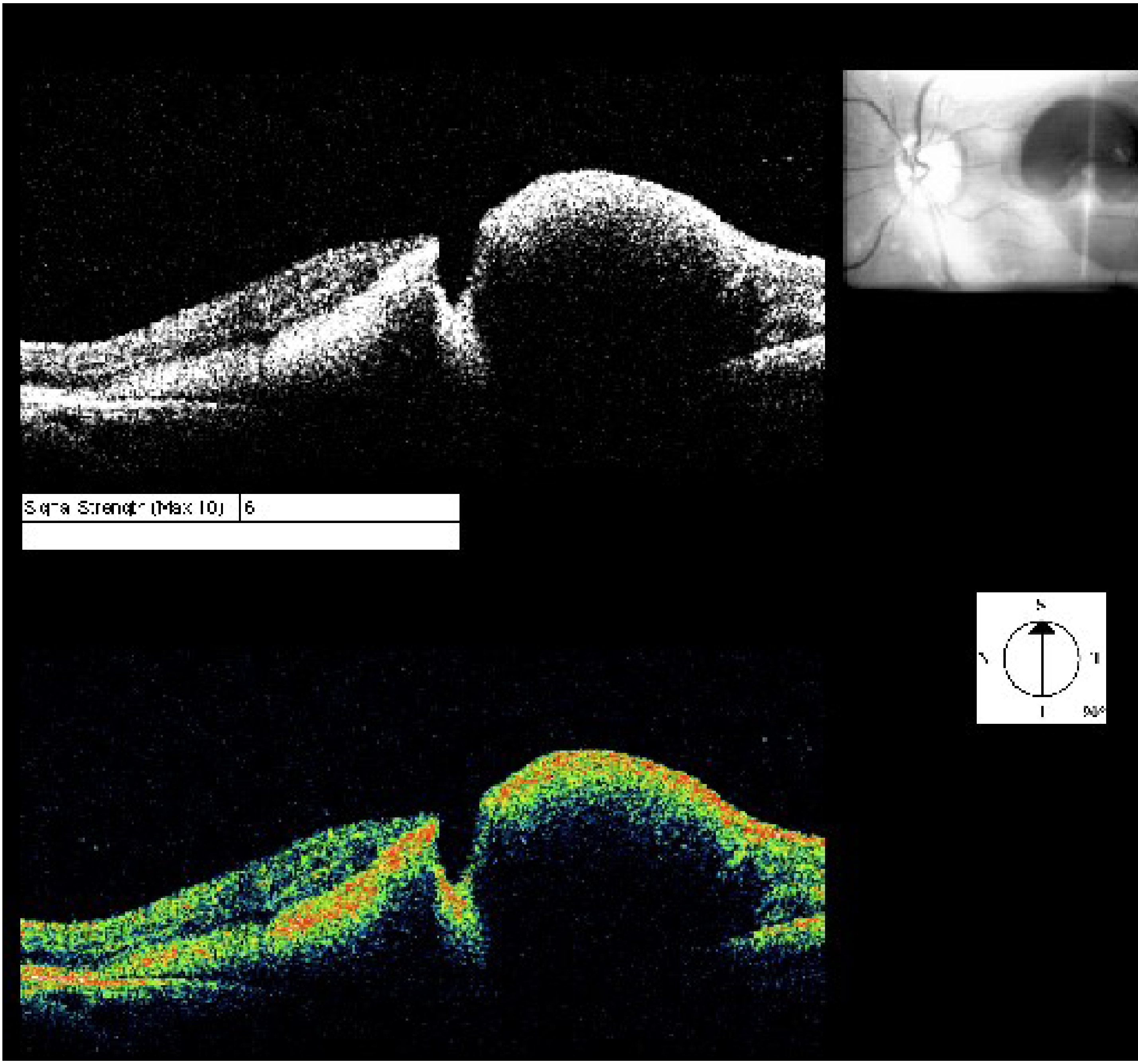


Figure 10. Optical coherence tomography (OCT). Raised area of the hemorrhage around the macroaneurysm.

DIFFERENTIAL DIAGNOSIS

Various clinical presentations of RAM with exudation and hemorrhage at many levels (pre-, sub- or intra-retinal) can simulate several conditions, such as other retinal vasculopathies, diabetic retinopathy, vein occlusions, some tumors (including retinal hemangiomas), choroid melanoma, and exudative AMD, which characterizes a "masked syndrome"[21,22]. Making a differential diagnosis becomes even more difficult because of the presence of vitreous or preretinal hemorrhage obscuring the lesion. Ultrasonography may reveal a lesion with tumor appearance, in which other typical characteristics of linear ultrasound (mode A) of choroid hemangiomas and melanomas are absent. The internal reflectivity is average and heterogeneous in the presence of massive subretinal hemorrhage associated with RAM.

Fluorescein angiography reveals the presence of hemorrhage around an artery with a typical dilated and hyperfluorescent lesion in the shape of a light bulb, contributing to the diagnosis of RAM. The presence of

multiple-level hemorrhage in one lesion suggests the presence of RAM, exudative AMD, and/or ischemic retinal vein occlusion.

OTHER ASSOCIATIONS

A syndrome characterized by retinal vasculitis, multiple macroaneurysms, neuroretinitis, and peripheral retinal ischemia (idiopathic retinal vasculitis, aneurysms, and neuro-retinitis) showed a correlation with RAM and other retinal findings. However, no systemic associations that contributed to the diagnosis were found[23].

PATHOLOGY

RAM solely comprises an anomaly of the arterial structure. Narrowing of the distal artery can be observed along with occasional occlusion of the arterial branch. Exudation and bleeding to the adjacent retina may also occur, along with protein deposits, lipid material, and hemosiderin in areas adjacent to RAM, retina, and subretinal space. Retinal capillaries are dilated around them. Clinically, these complications may lead to macular edema, serous retinal detachment, lipid deposition in a circinate pattern, and intra-retinal hemorrhages around the aneurysms[7,8].

TREATMENT AND PROGNOSIS

Natural history with satisfactory evolution without treatment has been widely studied, making the treatment of RAM a controversial subject[24,25]. Because many patients are asymptomatic and others show good progression with monitoring alone (Figure 11), the indication for treatment is restricted to complications such as macular exudation and hemorrhages with macular involvement or decreased vision[26,27].

Laser photocoagulation was one of the first treatments to be described with satisfactory results. Lasers with greater absorption by hemoglobin are usually preferred, such as those with wavelengths in the yellow spectrum, although therapeutic success has also been reported with other types of laser[28-31].

The proposed treatment is occlusion of the macroaneurysm. To this end, the suggestion is to continuously circle the lesion with wide beams (200–500 microns) and moderate intensity, possibly followed by direct application on the surface of the macroaneurysm with mild intensity and a beam of the size of the lesion[28].

Although conservative treatment is advocated by authors who have reported excellent prognosis with thrombosis and resorption of exudates, retinal structural damage may occur owing to edema or hemorrhage, leading to permanent low vision. There is no evidence supporting the advantage of using photocoagulation to treat macroaneurysms[28].

Although photocoagulation is indicated when exudation threatens the macula, complications such as vascular occlusion may occur, which are more severe the closer they are to the central area[28-31].

Anti-vascular endothelial growth factor therapy has been used alone or in association with photocoagulation for patients presenting with macular edema[45-47]. This treatment is safe and yields satisfactory results by reducing hemorrhage and edema (measured by OCT). It also improves visual acuity with only one application, in most cases[32].

Nd:Yag laser can also be used in cases of preretinal hemorrhage to perforate the posterior hyaloid and drain the hemorrhage into the vitreous cavity, clearing the visual axis and providing rapid improvement of the vision[35]. Although it can be performed in outpatient units, complications such as retinal perforation as well as development of epiretinal membranes and macular holes may occur[35-37].

The isolated injection of gas into the vitreous cavity can also be used for downward displacement of the hemorrhage to attempt the preservation of the photoreceptors and RPE in the macular region[38]. However, this technique should be performed within 24 hours of the appearance of the macroaneurysm, with the patient in the face-down position for 5 days for best results[38].

Pars plana vitrectomy has been reported as an option for the treatment of vitreous hemorrhage, both subhyaloidal and subretinal[39]. The use of adjuvants, such as tissue plasminogen activator, associated with pneumatic displacement of the hemorrhage or not[39] has been reported to facilitate the removal of subretinal blood, which is potentially toxic to the retinal pigment epithelium and photoreceptors and requires surgical removal[39-44]. In addition, vitrectomy can be diagnostic and therapeutic in cases of persistent vitreous hemorrhage, allowing the application of endophotocoagulation during surgery (Figure 12).

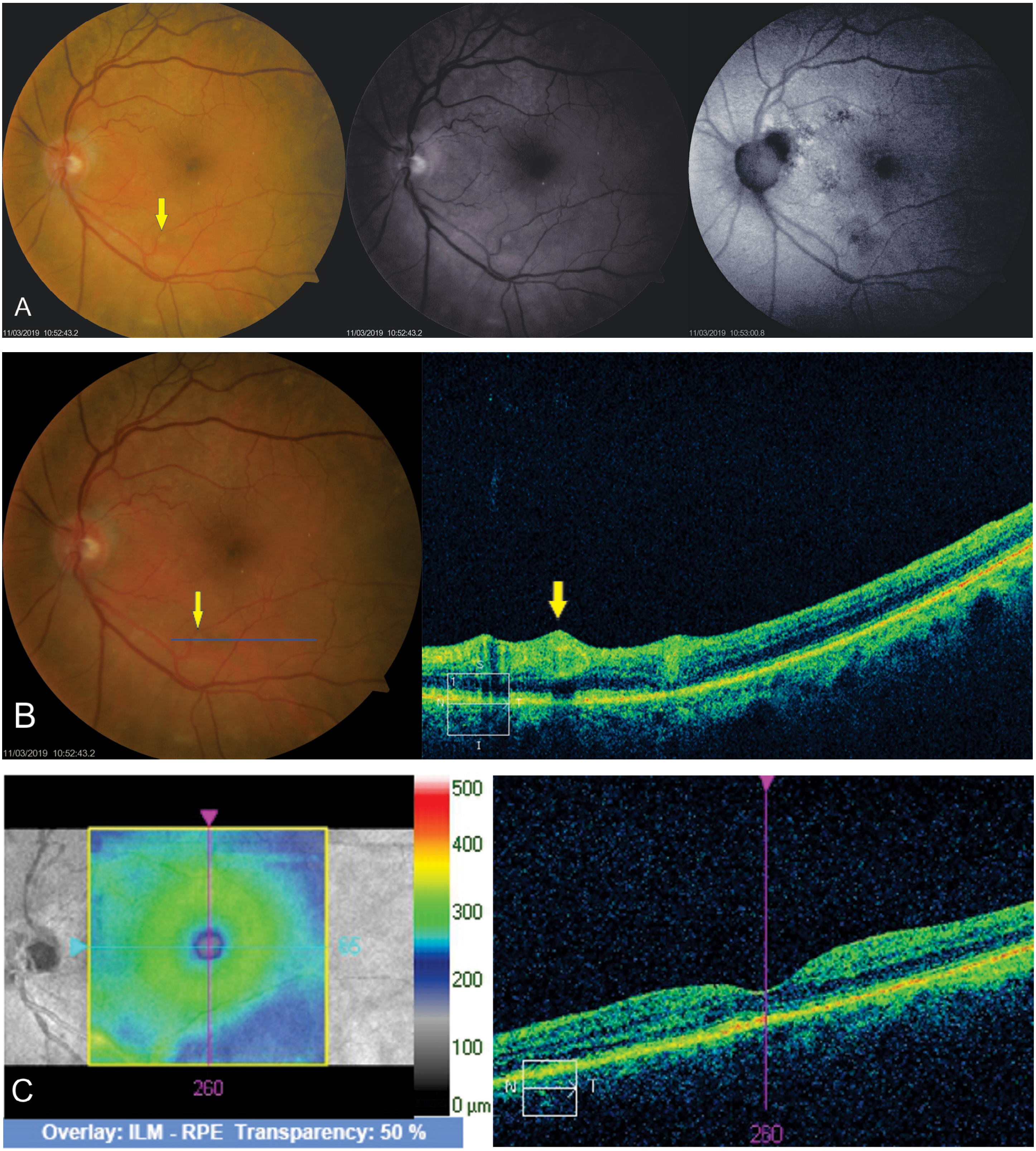


Figure 11. A) Color and red-free fundus photography and fundus autofluorescence of OS of an 86-year-old woman with hypertension, who presented with a loss of vision (VA = 20/40) owing to a lower temporal RAM (yellow arrow) associated with subretinal hemorrhage and slight lipid exudation around the lesion six months prior. Monitoring was suggested, after which, VA improved to 20/25, with complete resorption of the subretinal hemorrhage and hard exudates. B) Optical coherence tomography (OCT) showed the raised thrombosed RAM (yellow arrow) located between two other minor raised areas corresponding to the patient's retinal arteries in the same optical section (blue line). C) Macular tomographic section by OCT showing a normal anatomical profile and absence of intra- or subretinal exudation.

Figure 12. Postvitrectomy fundus photography (A) with endophotocoagulation for the treatment of vitreous hemorrhage and lipid exudation secondary to retinal arterial macroaneurysm. After 7 months of treatment (B), there was a significant reduction in retinal edema and hard exudates, and vision was regained.

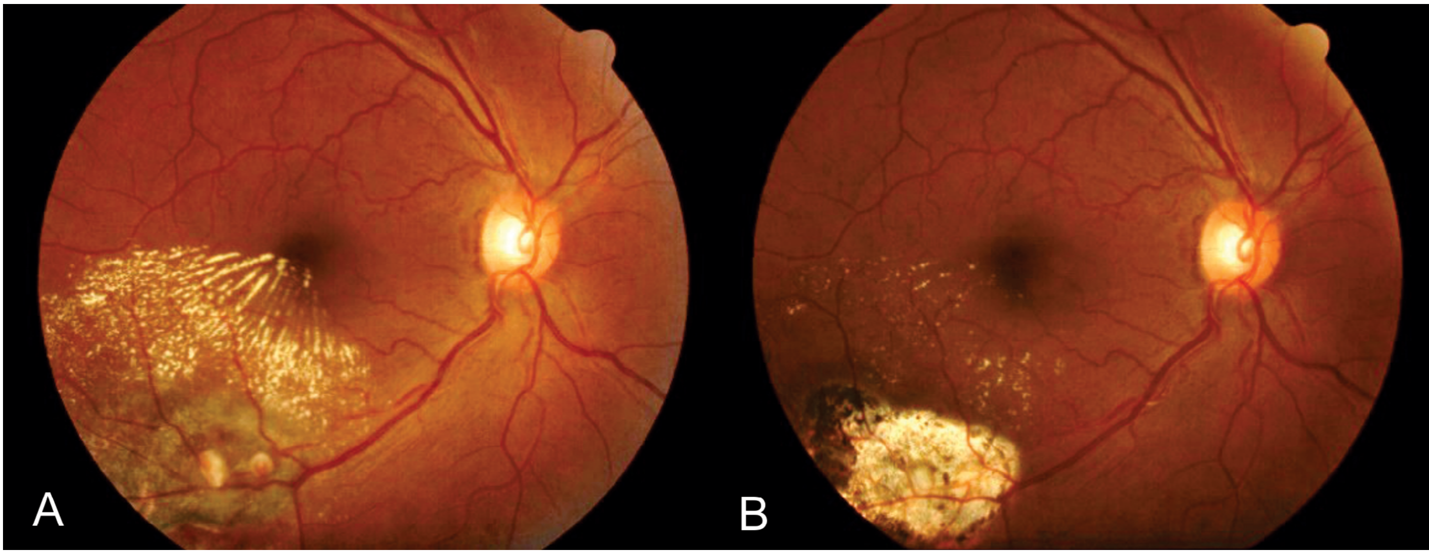


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In rare cases, rhegmatogenous retinal detachment, subretinal neovascular membranes, and macular holes, associated with subretinal hemorrhage or not, were reported as complications associated with the rupture of RAM[45].

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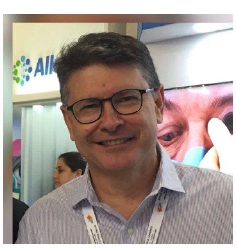
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